41. The method of Claim 31 wherein said vertebrate cells are mammalian cells.

42. The method of Claim 31 wherein said vertebrate cells are human cells.

43. A repressor complex, comprising two proteins having molecular weights of 35 and 42 kilodaltons, respectively, that binds to SEQ ID NO: 115 of the MN gene promoter.

44. The repressor complex of Claim 43 that binds to SEQ ID NO: 143 of the MN gene promoter.

REMARKS

To assist in the examination of this application and as required by 37 CFR 1.121, enclosed herewith as Appendix 1 is a marked up version of the changes made to the specification to indicate how the previous version of the specification has been modified to produce the clean replacement paragraphs. The modifications are indicated by underlining and in bold type for additions, and by strikeouts for deletions. Also enclosed as Appendix 2 is a clean set of all the claims now pending in accordance with 35 CFR 1.121(c)(3).

Specification

The Specification has been amended on page 5 to correct typographical/proofreading errors in lines 15 and 20. In line 15, the word "*the*" should not be in italics and in line 20, the word "identical" is inserted to replace the misspelled word "identicial".

The correction on page 26 is required in order to replace "Intron" with "Exon" in Table 1, line 4. Page 25, lines 10-15, of the instant application reads as follows:

> Exon-Intron Structure of Complete MN Genomic Region
>
> The complete sequence of the overlapping clones contains 10,898 bp (SEQ ID NO: 5). Figure 5 depicts the organization of the human MN gene, showing the location of all 11 exons as well as the 2 upstream and 6 intronic Alu repeat elements. All the exons are small, ranging from 27 to 191 bp, with the exception of the first exon which is 445 bp. The intron sizes range from 89 to 1400 bp.

[Emphasis added.] As the above quote shows, the MN gene contains 11 exons, and that the first exon contains 445 base pairs. The top section of Table 1 depicts 11 regions wherein the first region contains 445 base pairs. Further, the same Table 1 can be found in many of the issued U.S. MN patents including U.S. Patent 5,955,075. Table 1 (at column 18) of U.S. Patent No. 5,955,075 reads "Exon" on its fifth line. Applicants respectfully submit

that the amendment at page 26 of the instant application corrects a typographical, proofreading error that would be obvious to those of skill in the art.

The claims have been amended to point out with more particularity and clarity the subject matter regarded by the Applicants as their invention. Claims 20-27 and 31-44 are now pending in this National Stage application, and are shown in Appendix 2.

New Claims 31-42 are based on the cancelled originally filed PCT Claims 1-11. However, Claims 31-42 are method claims, whereas the cancelled Claims 1-11 are composition claims. Support in the Specification for such method claims can be found at least at page 6 (lines 4-9), page 7 (lines 5-12), page 20 (line 29) to page 21 (line 23), page 57 (lines 9-23), page 60 (line 29) to page 62 (line 7), and page 67 (line 28) to page 68 (line 20).

Claim 31 replaces originally filed Claim 1. Claims 32 and 34 replace Claims 3 and 4, respectively. Claim 33 is based on originally filed Claims 1 and 2.

Claims 35 and 36 are based on originally filed Claims 5 and 6, respectively. Claim 37 replaces claim 2 as originally filed. Claims 38-42 replace originally filed Claims 7-11, respectively.

New Claims 43 and 44 are based on originally filed Claims 28-30. Claim 43 replaces originally filed Claims 28, 29 and 30. Claim 44 is a new claim that is supported in the Specification at least at page 9 (lines 5-8) and page 28 (line 29) to page 29 (line 3).

Applicants respectfully conclude that no new matter has been entered by the above amendments.

CONCLUSION

Applicants respectfully submit that the claims as presented in this Preliminary Amendment are in condition for allowance, and earnestly request their prompt allowance. If the undersigned Attorney for the Applicants can be of any assistance in regard to the prosecution of this application, she can be reached at (415) 981-2034.

Respectfully submitted,

Leona L. Lauder
Attorney for Applicants
Registration No. 30,863

Dated: April 19, 2001

APPENDIX 1

The two paragraphs on page 5, lines 3-22 have been amended as follows:

MN/CA IX has a number of properties that distinguish it from other known CA isoenzymes and evince its relevance to oncogenesis. Those properties include its density dependent expression in cell culture (e.g., HeLa cells), its correlation with the tumorigenic phenotype of somatic cell hybrids between HeLa and normal human fibroblasts, its close association with several human carcinomas and its absence from corresponding normal tissues [e.g., Zavada et al., Int. J. Cancer, 54: 268-274 (1993); Pastorekova et al., Virology, 187: 620-626 (1992); Liao et al., Am. J. Pathol., 145: 598-609 (1994); Pastorek et al., Oncogene, 9: 2788-2888 (1994); Cote, Women's Health Weekly: News Section, p. 7 (March 30, 1998); Liao et al., Cancer Res., 57: 2827 (1997); Vermylen et al., "Expression of the MN antigen as a biomarker of lung carcinoma and associated precancerous conditions," Proceedings AACR, 39: 334 (1998); McKiernan et al., Cancer Res., 57: 2362 (1997); and Turner et al., Hum. Pathol., 28(6): 740 (1997)]. In addition, ~~the~~ **the** *in vitro* transformation potential of MN/CA IX cDNA has been demonstrated in NIH 3T3 fibroblasts [Pastorek et al., id.].

The MN protein has also been identified with the G250 antigen. Uemura et al., "Expression of Tumor-Associated Antigen MN/G250 in Urologic Carcinoma: Potential Therapeutic Target," J. Urol., 154 (4 Suppl.): 377 (Abstract 1475; 1997) states: "Sequence analysis and database searching revealed that G250 antigen is ~~identicial~~ **identical** to MN, a human tumor-associated antigen identified in cervical carcinoma (Pastorek et al., 1994)."

Table 1 on page 26 has been amended as follows:

TABLE 1

Exon-Intron Structure of the Human MN Gene

Exon ~~Intron~~	Size	Genomic Position**	SEQ ID NO	5'splice acceptor	SEQ ID NO
1	445	*3507-3951	28	AGAAG gtaagt	67
2	30	5126-5155	29	TGGAG gtgaga	68
3	171	5349-5519	30	CAGTC gtgagg	69
4	143	5651-5793	31	CCGAG gtgagc	70
5	93	5883-5975	32	TGGAG gtacca	71
6	67	7376-7442	33	GGAAG gtcagt	72
7	158	8777-8934	34	AGCAG gtgggc	73
8	145	9447-9591	35	GCCAG gtacag	74
9	27	9706-9732	36	TGCTG gtgagt	75
10	82	10350-70431	37	CACAG gtatta	76
11	191	10562-10752	38	ATAAT end	

Intron	Size	Genomic Position **	SEQ ID NO	3'splice acceptor	SEQ ID NO
1	1174	3952-5125	39	atacag GGGAT	77
2	193	5156-5348	40	ccccag GCGAC	78
3	131	5520-5650	41	acgcag TGCAA	79
4	89	5794-5882	42	tttcag ATCCA	80
5	1400	5976-7375	43	ccccag GAGGG	81
6	1334	7443-8776	44	tcacag GCTCA	82
7	512	8935-9446	45	ccctag CTCCA	83
8	114	9592-9705	46	ctccag TCCAG	84
9	617	9733-10349	47	tcgcag GTGACA	85
10	130	10432-10561	48	acacag AAGGG	86

** positions are related to nt numbering in whole genomic sequence including the 5' flanking region [Figure 2A-F]

* number corresponds to transcription initiation site determined below by RNase protection assay

APPENDIX 2

20. A vector comprising an expression control sequence operatively linked to a nucleic acid encoding the variable domains of a MN-specific antibody, wherein said domains are separated by a flexible linker polypeptide, and wherein said vector, when transfected into a vertebrate preneoplastic or neoplastic cell that abnormally expresses MN protein, inhibits the growth of said cell.

21. The vector of Claim 20 wherein said expression control sequence comprises the MN gene promoter operatively linked to said nucleic acid.

22. The vector of Claim 20 wherein said flexible linker polypeptide has the amino acid sequence of SEQ ID NO: 116.

23. The vector of Claim 20 wherein said expression control sequence comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 21, SEQ ID NO: 27 and SEQ ID NO: 91.

24. A vector comprising a nucleic acid that encodes a cytotoxic protein or cytotoxic polypeptide operatively linked to the MN gene promoter, wherein said vector, when transfected into a vertebrate preneoplastic or neoplastic cell that abnormally expresses MN protein, inhibits the growth of said cell.

25. The vector of Claim 24 wherein said cytotoxic protein is HSV thymidine kinase.

26. The vector according to Claim 24 wherein said vector further comprises a nucleic acid encoding a cytokine operatively linked to said MN gene promoter.

27. The vector of Claim 26 wherein said cytokine is interferon or interleukin-2.

31. A method of identifying an organic or an inorganic molecule that binds specifically to a site on a MN protein, to which vertebrate cells adhere in a cell adhesion assay, comprising testing organic and inorganic molecules in a cell adhesion assay, and identifying molecules that inhibit the adhesion of vertebrate cells to said MN protein as specifically binding to said site.

32. The method of Claim 31 wherein said molecule is organic.

33. The method of Claim 31 wherein said molecule is inorganic.

34. The method of Claim 32 wherein said molecule is a protein or a polypeptide.

35. The method of Claim 34 wherein said protein or polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 107, 108, 109, 137 and 138.

36. The method of Claim 32 wherein said polypeptide is selected from the group consisting of SEQ ID NOS: 107, 108, 109, 137 and 138.

37. The method of Claim 31 wherein said organic or inorganic molecule, when in contact with a vertebrate preneoplastic or neoplastic cell that abnormally expresses MN protein, inhibits the growth of said cell.

38. The method of Claim 31 wherein the site on the MN protein to which said vertebrate cells adhere in said cell adhesion assay is within the proteoglycan-like domain or within the carbonic anhydrase domain of the MN protein.

39. The method of Claim 31 wherein the site on the MN protein comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 10 and 97-106.

40. The method of Claim 31 wherein the site on the MN protein comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 10 and 97-106.

41. The method of Claim 31 wherein said vertebrate cells are mammalian cells.

42. The method of Claim 31 wherein said vertebrate cells are human cells.

43. A repressor complex, comprising two proteins having molecular weights of 35 and 42 kilodaltons, respectively, that binds to SEQ ID NO: 115 of the MN gene promoter.

44. The repressor complex of Claim 43 that binds to SEQ ID NO: 143 of the MN gene promoter.